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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,533	06/30/2003	Scott A. Waldman	100051.11211	4518
35148	7590	05/12/2009	EXAMINER	
Pepper Hamilton LLP 400 Berwyn Park 899 Cassatt Road Berwyn, PA 19312-1183		YU, MISOOK		
		ART UNIT		PAPER NUMBER
		1642		
		MAIL DATE		DELIVERY MODE
		05/12/2009		PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/611,533	WALDMAN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	MISOOK YU	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 25 February 2009.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-3,8-13,19,20,29-31 and 39-61 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-3,8-13,19,20,29-31,39,41,42,44,45,47-51,53-58 and 61 is/are rejected.
- 7) Claim(s) 40,43,46,52 and 59 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ .                                                        | 6) <input type="checkbox"/> Other: _____ .                        |

## **DETAILED ACTION**

Claims 1-3, 8-13, 19, 20, 29-31, 39-61 are pending and under consideration.

### ***Claim Objections, Withdrawn***

The objection of claims 41, 42, 44, 45, and 47 because of the incorporation of essential material in the specification by reference to a publication is withdrawn in view of the amendment.

### ***Claim Rejections - 35 USC § 112, Withdrawn***

The objection of claims 41, 42, 44, 45, 47 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in view of the amendment and the declaration executed by a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application would obviate this part of rejection.

### ***Claim Rejections - 35 USC § 103, Maintained***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 8-13, 19, 20, 29-31, and 39 remain rejected and new claims 49, 50, 53-57, 60, and 61 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Silberg et al., Gastroenterology, 1997 Aug;113(2):478-86 in view of US 5601990 A (the '990 patent, issue date of Feb. 11, 1997).

Claims 1-3, 8-13, 19, 20, 29-31, 39, new claims 49, 50, 53-57, 60, and 61 are drawn to method of screening an individual for metastatic colorectal, stomach or esophageal cancer comprising detection of CDX1 in extraintestinal tissue and/or body fluids.

Applicant argues that the metaplastic cells of Silberg are not same as metastatic cancer cells in the instant claims. The Office agrees with applicant that metaplastic cells are not same as metastatic cells.

Applicant argues that Silberg teaches away from using CDX1 as a marker in metastasized colorectal cancer cells or does not provide a reasonable expectation of success because of Silberg's teaching that "normal colonic epithelium stained intensely" for CDX1 while the staining decreased as the cells became more transformed as disclosed on page 482, right column, first full paragraph. Applicant also argues that Silberg teaches "some adenocarcinomas of the colon were devoid of CDX1 expression, whereas others had a small amount of staining." Applicant also argues that Silberg did not evaluate metastasized colorectal cancer cells in a sample from extraintestinal tissue and/or body fluids. Silberg's reporting that colon adenocarcinomas.

These arguments have been fully considered but found unpersuasive because Silberg teaches the following in the abstract:

CONCLUSIONS: CDX1 may be important in the transition from normal gastric and esophageal epithelium to intestinal-type metaplasia. The variability in expression of CDX1 in gastric and esophageal adenocarcinomas suggests more than one pathway in the development of these carcinomas. The decrease of CDX1 in colonic adenocarcinomas may indicate a role for CDX1 in growth regulation and in the maintenance of the differentiated phenotype.

Here, Silberg teaches “a possibility” of CDX1 being a marker for gastric and esophageal, and colon cancer. The instant claims as drafted say that presence of CDX1 expression indicates a possibility of metastatic colon, gastric or esophageal cancer. Therefore, the decreased expression taught by Silberg does not teach away from the instantly claimed invention. The instantly claimed invention encompasses decreased or increased expression. Only requirement in the instant claims is diction of CDX1 expression, not over-expression. As for extraintestinal sites, the ‘990 patent teaches that colon cancer cells are sometimes metastasized into extraintestinal sites, and grows in the new site. The ‘990 patent also teaches extraintestinal tissue (lymph node, note paragraph 31) and/or body fluids is used to detect a colon cancer biomarker and the detection of such biomarker for cancer is associated with metastasis. This indicates if a colon cancer biomarker shows up somewhere other than colon tissue, one of ordinary skill in the art would reasonably conclude that colon cancer cells are metastasized from its original location. Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention with a reasonable expectation of success since Silberg et al., teach that CDX1 is a biomarker “involved in the neoplastic process” (note page 479) of “Alimentary Tact Epithelium” (note the title) and the ‘990 patent teaches how to use extraintestinal tissue and/or body fluids for a biomarker for metastatic cancers. One of skill in the art would have been motivated to arrive at the claimed invention because US 5601990 at paragraph 6 teaches “diagnosis of metastatic or recurrent disease earlier potentially carries with it a better prognosis”.

Claims 41, 44, and 47 and new claims 51, and 58 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Silberg et al., (cited above) in view of US 5601990 A as applied to claims 1, 11, and 29 above, and further in view of GenBank Accession no. U51095 (Applicant provided a copy with the reply filed on 06/30/2008, 14-Jan-1997).

Note what Silberg et al., and US 5601990 A teach above.

Neither Silberg et al., nor US 5601990 A teach the claimed GenBank Accession no. U51095.

However, the GenBank Accession no. U51095 was known well before the effective filing date. Thus, this sequence would have been recognized by one of ordinary skill in the art as CDX1 of Silberg et al., above.

Therefore it would have been obvious to one of skill in the art to arrive at the claimed invention with a reasonable expectation of success since GenBank Accession no. U51095 teaches the necessary sequence information to make probes for the diction.

Claims 42, 45, and 48, and new claims 51, and 58 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Silberg et al., (cited above) in view of US 5601990 A as applied to claims 1, 11, and 29 above, and further in view of GenBank Accession no. U15212 (Applicant provided a copy with the reply filed on 06/30/2008, 14-Jan-1997).

Note what Silberg et al., and US 5601990 A teach above.

Neither Silberg et al., nor US 5601990 A teach the claimed GenBank Accession no. U15212.

However, the GenBank Accession no. U15212 was known well before the effective filing date. Thus, this sequence would have been recognized as CDX1 of Silberg et al., above.

Therefore it would have been obvious to one of skill in the art to arrive at the claimed invention with a reasonable expectation of success since GenBank Accession no. U15212 teaches the necessary sequence information to make probes for the diction.

***Conclusion***

Claims 40, 43, 46, 52, and 59 are objected to as being dependent upon a rejected base claim..

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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